

L Number	Hits	Search Text	DB	Time stamp
1	1276	multiplex\$4 NEAR (pcr amplification)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:02
2	162	((multiplex\$4 NEAR (pcr amplification)) and (Invader or taqman))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 16:56
3	15	((multiplex\$4 NEAR (pcr amplification)) and (Invader or taqman)) and ((hot near start) or (taqstart))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 16:57
4	4	((multiplex\$4 NEAR (pcr amplification)) and (Invader or taqman)) and ((hot near start) or (taqstart)) and (SNP or (single adj1 nucleotide adj1 polymorphism))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 16:58
5	0	((multiplex\$4 NEAR (pcr amplification)) and (at adj1 least adj1 ("50" or fifty)))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:03
6	35	((multiplex\$4 NEAR (pcr amplification)) and (at adj1 least adj5 primer))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:03
7	17	((multiplex\$4 NEAR (pcr amplification)) and (at adj1 least adj5 primer)) and (SNP or (single adj1 nucleotide adj1 polymorphism))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:06
8	18	((multiplex\$4 NEAR (pcr amplification)) and (at adj1 least adj5 primer)) not (((multiplex\$4 NEAR (pcr amplification)) and (at adj1 least adj5 primer)) and (SNP or (single adj1 nucleotide adj1 polymorphism)))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:39
13	59		USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:37
14	14		USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:39
15	2	("6489455").PN.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:39
16	0	((("6489455").PN.) and (SNP or (single adj1 nucleotide adj1 polymorphism)))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/10/02 17:39

FILE 'BIOSIS, MEDLINE, EMBAL, EMBASE, SCISEARCH, BIOTECHDS, CAPLUS'  
ENTERED AT 15:44:55 ON 02 OCT 2003

L1 40107 S SNP? OR (SINGLE (1W) NUCLEOTIDE (1W) POLYMORPHISM?)

L2 366 S L1 AND (INVADER? OR TAQMAN?)

L3 41 S L2 AND (MULTIPLEX)

L4 42 S L2 AND (MULTIPLEX?)

L5 0 S L4 AND (MULTIPLEX? (P) (AMPLIFICATION? PCR?))

L6 18 DUP REM L4 (24 DUPLICATES REMOVED)

L6 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:248267 CAPLUS

DOCUMENT NUMBER: 138:379797

TITLE: Genome-wide association study of bronchial asthma  
based on SNP analysis

AUTHOR(S): Tamati, Mayumi

CORPORATE SOURCE: Laboratory for Functional Analysis, SNP Research  
Center, The Institute of Physical and Chemical  
Research (RIKEN), Japan

SOURCE: Saishin Igaku (2003), 58(2), 209-215

CODEN: SAIGAK; ISSN: 0370-8241

PUBLISHER: Saishin Igakusha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

TI Genome-wide association study of bronchial asthma based on SNP  
analysis

AB A review gives an overview of genome-wide genetic linkage study of  
bronchial asthma based on SNP anal. Development of  
establishment of database genome-wide SNP information for  
Japanese population was summarized. Current status of the SNP  
anal. and linkage anal. for identifying asthma-related genes in Japan was  
discussed. The advantage of the use of the Multiplex PCR and  
the Invader methods in collecting SNP information was  
described.

ST review genome wide SNP genetic linkage analysis bronchial asthma

IT Databases

(SNP database; genome-wide assocn. study of bronchial asthma  
based on SNP anal.)

IT Gene, animal

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(assocd. with bronchial asthma; genome-wide assocn. study of bronchial  
asthma based on SNP anal.)

IT Asthma

Genetic linkage

Human

(genome-wide assocn. study of bronchial asthma based on SNP  
anal.)

IT Genetic polymorphism

(single nucleotide; genome-wide assocn. study of bronchial asthma based on SNP anal.)

L6 ANSWER 2 OF 18 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN  
ACCESSION NUMBER: 2003:70704 SCISEARCH  
THE GENUINE ARTICLE: 634QF

TITLE: Improved sensitivity for solid-support invasive cleavage  
reactions with flow cytometry analysis

AUTHOR: Stevens P W (Reprint); Rao K V N; Hall J G; Lyamichev V;  
Neri B P; Kelso D M

CORPORATE SOURCE: Northwestern Univ, Robert R McCormick Sch Engr & Appl  
Sci,

Dept Biomed Engr, 2145 Sheridan Rd, Evanston, IL 60208 USA  
(Reprint); Northwestern Univ, Robert R McCormick Sch Engr  
& Appl Sci, Dept Biomed Engr, Evanston, IL 60208 USA;  
Third Wave Technol, Madison, WI USA

COUNTRY OF AUTHOR: USA

SOURCE: BIOTECHNIQUES, (JAN 2003) Vol. 34, No. 1, pp. 198-203.  
Publisher: EATON PUBLISHING CO, 154 E. CENTRAL ST, NATICK,  
MA 01760 USA.  
ISSN: 0736-6205.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 15

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB . . . nucleotide differences at target concentrations less than 200  
fm. This sensitivity level is within the range required for analysis of  
SNPs in genomic DNA. In addition, the flow cytometry format has  
multiplexing potential, making the microsphere-based invasive  
cleavage assay attractive for high throughput genomic applications.  
STP KeyWords Plus (R): SIGNAL AMPLIFICATION REACTION;  
OLIGONUCLEOTIDE PROBES;  
INVADER ASSAY; IDENTIFICATION; DNA; PLATFORM

L6 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:136073 CAPLUS

DOCUMENT NUMBER: 136:196564

TITLE: Non-fluorescent asymmetric cyanine dye compounds  
useful for quenching reporter dyes

INVENTOR(S): Lee, Linda G.; Graham, Ronald J.; Mullah, Khairuzzaman  
B.; Haxo, Francis T.

PATENT ASSIGNEE(S): PE Corporation (NY), USA

SOURCE: U.S., 62 pp., Cont.-in-part of U.S. 6,080,868.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348596	B1	20020219	US 1999-357740	19990720
US 6080868	A	20000627	US 1998-12525	19980123
US 6541618	B1	20030401	US 2000-602544	20000621
PRIORITY APPLN. INFO.:			US 1998-12525	A2 19980123
OTHER SOURCE(S):	MARPAT 136:196564			
REFERENCE COUNT:	84	THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS		

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The invention provides asym. cyanine dye compds. I, including substituted forms thereof, which are non-fluorescent quencher mols. The invention further provides reporter-quencher dye pairs, wherein the asym. cyanine dyes are the quenchers, polynucleotides incorporating the asym. cyanine dyes, and nucleic acid hybridization detection methods utilizing the dye-labeled polynucleotides. Nitrothiazole blue XXXIV was prepd. from 2-methylbenzothiazole and used as a quencher dye paired with FAM or TET reporter dyes in Taqman assays.

ST asym cyanine dye fluorescence quenching reagent; nucleic acid hybridization asym cyanine dye fluorescence quencher; nitrothiazole blue quencher dye Taqman assay

IT PCR (polymerase chain reaction)  
(Taqman assay, doubly-labeled probe for; non-fluorescent asym. cyanine dye compds. useful for quenching reporter dyes)

IT Gene, animal  
RL: ANT (Analyte); ANST (Analytical study)  
(for .beta.-actin of human, Taqman assay for; non-fluorescent asym. cyanine dye compds. useful for quenching reporter dyes)

IT PCR (polymerase chain reaction)  
(multiplex; non-fluorescent asym. cyanine dye compds. useful for quenching reporter dyes)

IT Actins  
RL: ANT (Analyte); ANST (Analytical study)  
(.beta.-, Taqman assay for human gene for; non-fluorescent asym. cyanine dye compds. useful for quenching reporter dyes)

IT 400185-16-2 400185-17-3 400185-18-4 400185-19-5 400185-20-8 400185-21-9  
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)  
(nucleotide sequence, SNP primer; non-fluorescent asym. cyanine dye compds. useful for quenching reporter dyes)

ACCESSION NUMBER: 2002:784266 CAPLUS  
 DOCUMENT NUMBER: 137:305690  
 TITLE: High-throughput single-nucleotide  
 polymorphism typing system by  
 multiplex PCR-Invader assay  
 INVENTOR(S): Nakamura, Yusuke; Tanaka, Toshihiro; Onishi, Yozo;  
 Ozaki, Koichi; Yamada, Akira  
 PATENT ASSIGNEE(S): Institute of Physical and Chemical Research, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 45 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002300894	A2	20021015	JP 2002-19752	20020129
US 2002182622	A1	20021205	US 2002-60301	20020201

PRIORITY APPLN. INFO.: JP 2001-25700 A 20010201  
 T1 High-throughput single-nucleotide polymorphism  
 typing system by multiplex PCR-Invader assay  
 AB A method for genotyping of single-nucleotide  
 polymorphisms (SNPs) by nucleic acid amplification with  
 a large no. of primers, is disclosed. Hot-start PCR, Taqman  
 PCR, or invader method, may be preferably used. One of the most  
 difficult issues to be solved in genome-wide assocn. studies is to reduce  
 the amt. of genomic DNA required for genotyping. Currently available  
 technologies require too large a quantity of genomic DNA to genotype with  
 hundreds or thousands of single-nucleotide  
 polymorphisms (SNPs). To overcome this problem, the  
 authors combined the Invader assay with multiplex  
 polymerase chain reaction (PCR), carried out in the presence of antibody  
 to Taq polymerase, as well as using a novel 384-well card system that can  
 reduce the required reaction vol. The authors amplified 100 genomic DNA  
 fragments, each contg. one SNP, in a single tube, and analyzed  
 each SNP with the Invader assay. This procedure  
 correctly genotyped 98 of the 100 SNP loci examd. in  
 PCR-amplified samples from ten individuals; the genotypes were confirmed  
 by direct sequencing. The reproducibility and universality of the method  
 were confirmed with two addnl. sets of 100 SNPs. Because the  
 authors used 40ng of genomic DNA as a template for multiplex  
 PCR, the amt. needed to assay one SNP was only 0.4 ng;  
 therefore, theor., more than 200,000 SNPs could be genotyped at  
 once when 100 .mu.g of genomic DNA is available. Our results indicate the  
 feasibility of undertaking genome-wide assocn. studies using blood samples

of only 5-10mL.

L6 ANSWER 5 OF 18 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2002704237 MEDLINE  
DOCUMENT NUMBER: 22353531 PubMed ID: 12465410  
TITLE: A high-throughput SNP typing system for  
genome-wide association studies.  
AUTHOR: Ohnishi Yozo  
CORPORATE SOURCE: Laboratory for Cardiovascular Diseases, SNP Research  
Center, Institute of Physical and Chemical Research  
(RIKEN), 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639,  
Japan.  
SOURCE: GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER  
AND  
CHEMOTHERAPY], (2002 Nov) 29 (11) 2031-6.  
Journal code: 7810034. ISSN: 0385-0684.  
PUB. COUNTRY: Japan  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Japanese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200212  
ENTRY DATE: Entered STN: 20021217  
Last Updated on STN: 20021218  
Entered Medline: 20021213

TI A high-throughput SNP typing system for genome-wide association  
studies.  
AB SNPs are useful markers for identifying genes responsible for  
and/or associated with common diseases, and for directing personalized  
medical care. Furthermore, because they are so frequent in the genome and  
can be genotyped quite easily, SNPs can serve as markers for a  
whole genome association study. However, one of the most difficult issues  
to be solved for whole-genome association studies using SNPs is  
reduction of the amount of genomic DNA for genotyping. The presently  
available technologies require too much genomic DNA to be practical. To  
overcome this problem, we combined the Invader assay with  
multiplex PCR performed in the presence of Taq polymerase antibody  
as well as a novel 384-well card system that reduces the reaction volume.  
We amplified 96 genomic DNA fragments simultaneously in a single tube, and  
analyzed each SNP using the Invader assay. Since we  
used 10-20 nanograms of genomic DNA as a template for multiplex  
PCR, the amount needed to assay one SNP was only 0.1-0.2  
nanograms. Our results strongly indicate the feasibility of undertaking  
genome-wide association studies using blood samples of only. . .

L6 ANSWER 6 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC. on STN

ACCESSION NUMBER: 2002:616684 BIOSIS

DOCUMENT NUMBER: PREV200200616684

TITLE: A high-throughput SNP typing system for  
genome-wide association studies in patients with myocardial  
infarction.

AUTHOR(S): Ohnishi, Y. (1); Tanaka, T. (1); Ozaki, K. (1); Sekine, A.  
(1); Nakamura, Y. (1)

CORPORATE SOURCE: (1) SNP Research Ctr, RIKEN, Tokyo Japan  
SOURCE: American Journal of Human Genetics, (October, 2002) Vol.  
71, No. 4 Supplement, pp. 435.  
<http://www.journals.uchicago.edu/AJHG/home.html>. print.  
Meeting Info.: 52nd Annual Meeting of the American Society  
of Human Genetics Baltimore, MD, USA October 15-19, 2002  
American Society of Human Genetics  
. ISSN: 0002-9297.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI A high-throughput SNP typing system for genome-wide association  
studies in patients with myocardial infarction.

IT Methods & Equipment

Invader assay; assessment method; genotyping;  
characterization method; high-throughput SNP typing system;  
laboratory equipment; multiplex PCR

IT Miscellaneous Descriptors

genome-wide association; Meeting Abstract

L6 ANSWER 7 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON

DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01265 BIOTECHDS

TITLE: Rapid multiplex single nucleotide  
polymorphism genotyping based on single base  
extension reactions and color-coded beads;  
SNP genotyping using microphore bead washing  
after polymerase chain reaction

AUTHOR: FUJIMURA N; KOHARA Y; OKANO K; YOHDA M; KAMBARA H

CORPORATE SOURCE: Tokyo Univ Agr and Technol; Hitachi Ltd

LOCATION: Kohara Y, Tokyo Univ Agr and Technol, Dept Biotechnol and  
Life Sci, 2-24-16 Nakacho, Koganei, Tokyo 1840012, Japan

SOURCE: JOURNAL OF BIOSCIENCE AND BIOENGINEERING; (2002) 94,  
4,

368-370

ISSN: 1389-1723

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Rapid multiplex single nucleotide

polymorphism genotyping based on single base extension reactions

and color-coded beads;

SNP genotyping using microphore bead washing after  
polymerase chain reaction

AB AUTHOR ABSTRACT - A Single nucleotide  
polymorphism (SNP) typing method using color-coded  
beads is promising because it is easy to use and inexpensive. However,  
the present protocols are . . . diagnostic applications because they  
need centrifugation for bead-washing. Here, we developed a simplified  
protocol without a bead-washing procedure that enables SNP  
typing of PCR amplified fragments in only 30 min.

DERWENT ABSTRACT: SNPs are the most frequent DNA polymorphism  
found. They are expected to be diagnosis markers for a number of diseases  
and drug responses. Many SNP typing methods, including the  
TaqMan assay, Invader assay, molecular beacon,  
polymerase chain reaction and electrophoresis, mass spectrometry,  
pyro-DNA sequencing, bioluminometric assay coupled with modified primer  
extension reactions, DNA chip, and bead technology, have been developed.  
The paper looks at a rapid and simplified SNP typing method  
using single base extension reactions and color-coded beads(3 pages)

CT SNP, GENOTYPING, SINGLE BASE EXTENSION, POLYMERASE CHAIN  
REACTION, MICROSPHERE BEAD, DNA PRIMER, FLOW CYTOMETRY  
ANALYSIS, APPL.  
DIAGNOSIS DNA AMPLIFICATION HYBRIDIZATION (22,. . .

L6 ANSWER 8 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS  
RESERVED.

on STN

ACCESSION NUMBER: 2002085075 EMBASE

TITLE: High-throughput SNP genotyping.

AUTHOR: Jenkins S.; Gibson N.

CORPORATE SOURCE: S. Jenkins, R and D Genetics, AstraZeneca, Mereside,  
Alderley Park, Macclesfield, Cheshire SK10 4TG, United  
Kingdom. suzanne.jenkins@astrazeneca.com

SOURCE: Comparative and Functional Genomics, (2002) 3/1 (57-66).

Refs: 46

ISSN: 1531-6912 CODEN: YESTE3

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

027 Biophysics, Bioengineering and Medical  
Instrumentation

LANGUAGE: English

SUMMARY LANGUAGE: English

TI High-throughput SNP genotyping.

AB Whole genome approaches using single nucleotide  
polymorphism (SNP) markers have the potential to



transform complex disease genetics and expedite pharmacogenetics research. This has led to a requirement for high-throughput SNP genotyping platforms. Development of a successful high-throughput genotyping platform depends on coupling reliable assay chemistry with an appropriate detection system. . . only a few cents per genotype. In addition, DNA template requirements must be minimised such that hundreds of thousands of SNPs can be interrogated using a relatively small amount of genomic DNA. As such, it is predicted that the next generation of high-throughput genotyping platforms will exploit large-scale multiplex reactions and solid phase assay detection systems.  
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L6 ANSWER 9 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:390975 BIOSIS

DOCUMENT NUMBER: PREV200300390975

TITLE: A multiplex solution for SNP  
interrogation using fifth-dye labeled short size standard  
and single-tube primer extension reaction.

AUTHOR(S): Kuo, S. S. (1); Wei, D. (1); Ayanoglu, G. (1); Johnson, M.  
(1); Chang, C. (1); Hanachi, P. (1); Tomaney, A. B. (1);  
Dong, P. (1)

CORPORATE SOURCE: (1) Applied Biosystems, Foster City, CA, USA:  
kuoss@appliedbiosystems.com USA

SOURCE: European Journal of Human Genetics, (2001) Vol. 9, No.  
Supplement 1, pp. P1238. print.  
Meeting Info.: 10th International Congress of Human  
Genetics Vienna, Austria May 15-19, 2001 International  
Federation of Human Genetics Societies  
. ISSN: 1018-4813.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI A multiplex solution for SNP interrogation using  
fifth-dye labeled short size standard and single-tube primer extension  
reaction.

IT . . .  
techniques, laboratory techniques; fifth-dye labeled short size  
standard extension reaction: genetic techniques, laboratory techniques;  
genotyping: genetic techniques, laboratory techniques; real-time  
Taqman PCR analysis [real-time Taqman polymerase  
chain reaction analysis]: genetic techniques, laboratory techniques;  
single-tube primer extension reaction: laboratory techniques

IT Miscellaneous Descriptors  
SNP [single nucleotide  
polymorphisms]; multiplex solution; Meeting Abstract

L6 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 2

ACCESSION NUMBER: 2001:409593 BIOSIS

DOCUMENT NUMBER: PREV200100409593

TITLE: A high-throughput SNP typing system for  
genome-wide association studies.

AUTHOR(S): Ohnishi, Yozo; Tanaka, Toshihiro; Ozaki, Kouichi; Yamada,  
Ryo; Suzuki, Hideyuki; Nakamura, Yusuke (1)

CORPORATE SOURCE: (1) Laboratory of Molecular Medicine, Human Genome  
Center,

Institute of Medical Science, University of Tokyo, 4-6-1

Shirokanedai, Minato-ku, Tokyo, 108-8639:

yusuke@ims.u-tokyo.ac.jp Japan

SOURCE: Journal of Human Genetics, (2001) Vol. 46, No. 8, pp.

471-477. print.

ISSN: 1434-5161.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

TI A high-throughput SNP typing system for genome-wide association  
studies.

AB. . . for genotyping. Currently available technologies require too large a  
quantity of genomic DNA to genotype with hundreds or thousands of  
single-nucleotide polymorphisms (SNPs

). To overcome this problem, we combined the Invader assay with  
multiplex polymerase chain reaction (PCR), carried out in the  
presence of antibody to Taq polymerase, as well as using a novel 384-well  
card system that can reduce the required reaction volume. We amplified 100  
genomic DNA fragments, each containing one SNP, in a single  
tube, and analyzed each SNP with the Invader assay.

This procedure correctly genotyped 98 of the 100 SNP loci  
examined in PCR-amplified samples from ten individuals; the genotypes were  
confirmed by direct sequencing. The reproducibility and universality of  
the method were confirmed with two additional sets of 100 SNPs.

Because we used 40 ng of genomic DNA as a template for multiplex  
PCR, the amount needed to assay one SNP was only 0.4 ng;  
therefore, theoretically, more than 200,000 SNPs could be  
genotyped at once when 100 mug of genomic DNA is available. Our results  
indicate the feasibility of undertaking. . .

L6 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 3

ACCESSION NUMBER: 2001:214630 BIOSIS

DOCUMENT NUMBER: PREV200100214630

TITLE: High-throughput multiplex SNP  
genotyping with MALDI-TOF mass spectrometry: Practice,  
problems and promise.  
AUTHOR(S): Bray, Molly S. (1); Boerwinkle, Eric; Doris, Peter A.  
CORPORATE SOURCE: (1) Human Genetics Center, University of Texas Health  
Science Center at Houston, Houston, TX, 77225:  
molly.s.bray@uth.tmc.edu USA  
SOURCE: Human Mutation, (2001) Vol. 17, No. 4, pp. 296-304. print.  
ISSN: 1059-7794.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

TI High-throughput multiplex SNP genotyping with

MALDI-TOF mass spectrometry: Practice, problems and promise.

AB Single nucleotide polymorphisms (

SNPs) are currently being identified and mapped at a remarkable  
pace, providing a rich genetic resource with vast potential for disease.  
. . . humans. High-throughput, cost effective genotyping methods are  
essential in order to make the most advantageous and immediate use of  
these SNP data. We have incorporated the use of matrix-assisted  
laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF)  
in our laboratory as a tool. . . for differentiating genotypes based on  
the mass of the variant DNA sequence, and have utilized this method for  
production scale SNP genotyping. We have combined a 4 mul PCR  
amplification reaction using 3 ng of genomic DNA with a secondary  
enzymatic. . . analysis of mini-sequencing reactions was performed  
using a MALDI-TOF instrument (Voyager-DE, Perseptive Biosystems,  
Framingham, MA). We performed both single and multiplex PCR and  
mini-sequencing reactions, and genotyped seven different variant sites in  
a random sample of 989 individuals. Genotypes generated with MS methods  
were compared with genotypes produced using a 5' exonuclease  
fluorescence-based assay (Taqman, Applied Biosystems, Foster  
City, CA) and a gel-based genotyping protocol. Because multiple  
polymorphisms can be detected in a single reaction,. . .

L6 ANSWER 12 OF 18 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2001156126 MEDLINE

DOCUMENT NUMBER: 21098045 PubMed ID: 11159763

TITLE: Enabling large-scale pharmacogenetic studies by  
high-throughput mutation detection and genotyping  
technologies.

AUTHOR: Shi M M

CORPORATE SOURCE: Department of Applied Genomics, Genometrix Inc., The  
Woodlands, TX 77381, USA.. mshi@genometrix.com

SOURCE: CLINICAL CHEMISTRY, (2001 Feb) 47 (2) 164-72. Ref: 40  
Journal code: 9421549. ISSN: 0009-9147.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200103  
ENTRY DATE: Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered Medline: 20010322

AB . . . challenge. APPROACH: This article reviews the recent technology development in mutation detection and genotyping with a focus on genotyping of single nucleotide polymorphisms (SNPs). CONTENT: Novel mutations/polymorphisms are commonly identified by conformation-based mutation screening and direct high-throughput heterozygote sequencing. With a large amount of public sequence information available, in silico SNP mapping has also emerged as a cost-efficient way for new polymorphism identification. Gel electrophoresis-based genotyping methods for known polymorphisms include PCR coupled with restriction fragment length polymorphism analysis, multiplex PCR, oligonucleotide ligation assay, and minisequencing. Fluorescent dye-based genotyping technologies are emerging as high-throughput genotyping platforms, including oligonucleotide ligation assay, pyrosequencing, single-base extension with fluorescence detection, homogeneous solution hybridization such as TaqMan, and molecular beacon genotyping. Rolling circle amplification and Invader assays are able to genotype directly from genomic DNA without PCR amplification. DNA chip-based microarray and mass spectrometry genotyping technologies. . .

L6 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 5

ACCESSION NUMBER: 2001:125349 BIOSIS

DOCUMENT NUMBER: PREV200100125349

TITLE: An improved real time PCR method for simultaneous detection of C282Y and H63D mutations in the HFE gene associated with hereditary hemochromatosis.

AUTHOR(S): Walburger, D. K. (1); Afonina, I. A.; Wydro, R.

CORPORATE SOURCE: (1) Epoch Biosciences, 12277 134th Ct NE, No. 110, Redmond,

WA, 98052; dwalburger@epochpharm.com USA

SOURCE: Mutation Research, (January, 2001) Vol. 432, No. 3-4, pp. 69-78, print.

ISSN: 0027-5107.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB. . . HFE gene-C282Y and H63D-are associated with greater than 90% of HH cases. We have developed a sensitive real time PCR (TaqMan) 5'-nuclease assay for single nucleotide polymorphism (SNP) detection using novel DNA chemistry, and successfully applied this method to detect these mutations. Fluorogenic PCR probes, chemically modified with a minor groove binding agent to increase duplex stability, were used in single and multiplex probe closed tube formats. The probes were tested in two commercially available thermocycling fluorimeters (the Light Cycler™ and the ABI. . .

L6 ANSWER 14 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:151558 BIOSIS

DOCUMENT NUMBER: PREV200100151558

TITLE: Enabling large-scale pharmacogenetic studies by high-throughput mutation detection and genotyping technologies.

AUTHOR(S): Shi, Michael M. (1)

CORPORATE SOURCE: (1) Genometrix Inc., 2700 Research Forest Dr., The Woodlands, TX, 77381: mshi@genometrix.com USA

SOURCE: Clinical Chemistry, (February, 2000) Vol. 47, No. 2, pp. 164-172. print.

ISSN: 0009-9147.

DOCUMENT TYPE: General Review

LANGUAGE: English

SUMMARY LANGUAGE: English

AB. . . challenge. Approach: This article reviews the recent technology development in mutation detection and genotyping with a focus on genotyping of single nucleotide polymorphisms (SNPs). Content: Novel mutations/polymorphisms are commonly identified by conformation-based mutation screening and direct high-throughput heterozygote sequencing. With a large amount of public sequence information available, in silico SNP mapping has also emerged as a cost-efficient way for new polymorphism identification. Gel electrophoresis-based genotyping methods for known polymorphisms include PCR coupled with restriction fragment length polymorphism analysis, multiplex PCR, oligonucleotide ligation assay, and minisequencing. Fluorescent dye-based genotyping technologies are emerging as high-throughput genotyping platforms, including oligonucleotide ligation assay, pyrosequencing, single-base extension with fluorescence detection, homogeneous solution hybridization such as TaqMan(R), and molecular beacon genotyping. Rolling circle amplification and Invader™ assays are able to genotype directly from genomic DNA

without PCR amplification. DNA chip-based microarray and mass spectrometry genotyping technologies. . .

L6 ANSWER 15 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
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DUPLICATE 6

ACCESSION NUMBER: 2000:360537 BIOSIS

DOCUMENT NUMBER: PREV200000360537

TITLE: Suspension arrays for high throughput, multiplexed  
single nucleotide polymorphism  
genotyping.

AUTHOR(S): Armstrong, Barbara; Stewart, Michael; Mazumder, Abhijit (1)

CORPORATE SOURCE: (1) Motorola Biochip Systems, 4088 Commercial Ave.,  
Northbrook, IL, 60062 USA

SOURCE: Cytometry, (June 1, 2000) Vol. 40, No. 2, pp. 102-108.  
print.

ISSN: 0196-4763.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

TI Suspension arrays for high throughput, multiplexed  
single nucleotide polymorphism genotyping.

AB. . . Background: Genetic diversity can help explain disease susceptibility and differential drug response. The most common type of variant is the single nucleotide polymorphism (SNP). We present a low-cost, high throughput assay for SNP genotyping. Methods: The assay uses oligonucleotide probes covalently attached to fluorescently encoded microspheres. These probes are hybridized directly to fluorescently. . . in a standard flow cytometer. Results: The genotypes determined with our assay are in good agreement with those determined by TaqMan. The range of G/C content for oligonucleotide probes was 23.5-65% in the 17 bases surrounding the SNP. Further optimization of probe length and target concentration is shown to dramatically enhance the assay performance for certain SNPs. Using microspheres which have unique fluorescent signatures, we performed a 32-plex assay where we simultaneously determined the genotypes of eight different polymorphic genes. Conclusions: We demonstrate, for the first time, the feasibility of multiplexed genotyping with suspension arrays using direct hybridization analyses. Our approach enables probes to be removed from or added to an array, enhancing flexibility over conventional chips. The ability to multiplex both the PCR preparation and the hybridization should enhance the throughput, cost, and speed of the assay.

L6 ANSWER 16 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
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ACCESSION NUMBER: 2001:528511 BIOSIS

DOCUMENT NUMBER: PREV200100528511

TITLE: A single-tube primer extension reaction enabling  
multiplex SNP interrogation.

AUTHOR(S): Wei, Dong (1); Johnson, Martin (1); Kuo, Sophia (1);  
Hanachi, Parisa (1); Yu, Wendy (1); Dong, Penny (1)

CORPORATE SOURCE: (1) Applied Biosystems, Foster City, CA USA

SOURCE: International Genome Sequencing and Analysis Conference,  
(2000) Vol. 12, pp. 96-97. print.  
Meeting Info.: 12th International Genome Sequencing and  
Analysis Conference Miami Beach, Florida, USA September  
12-15, 2000

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

TI A single-tube primer extension reaction enabling multiplex  
SNP interrogation.

AB A variety of methods may be used to characterize and screen for  
single nucleotide polymorphisms. Analysis  
platforms include microarray scanning, real time PCR analysis (Taqman) and MALDI-TOF. Additionally, electrophoresis based techniques include OLA analysis, dideoxy sequencing and single-nucleotide primer extension (e.g., SNaPshot). SNaPshot is a single-tube reaction designed for elucidation of individual loci within known sequence contexts for the purpose of SNP screening. The reaction is designed as a premix that contains all of the components except primers and templates. The completed . . . identifies one nucleotide located 3' relative to the primer site. We have reformulated our SNaPshot reagent mix to enable robust multiplex SNP interrogation against multiple templates in varying amounts. The resulting multiple products can then be analyzed by electrophoresis in the presence. . .

L6 ANSWER 17 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC. on STN

ACCESSION NUMBER: 2001:494471 BIOSIS

DOCUMENT NUMBER: PREV200100494471

TITLE: Multiplexed genotyping assay that combines a  
novel labeling strategy with microchannel electrophoresis.

AUTHOR(S): Cronin, Maureen T. (1); Williams, Stephen J. (1); Pho,  
Mylan (1); Wei, Jing (1); Leon, Suzan (1); Matray, Tracy  
(1); Singh, Sharat (1); Livak, Ken J.; Dong, Penny;  
Mansfield, Elaine S. (1)

CORPORATE SOURCE: (1) ACLARA BioSciences Inc., Mountain View, CA USA

SOURCE: International Genome Sequencing and Analysis Conference,  
(2000) Vol. 12, pp. 27. print.  
Meeting Info.: 12th International Genome Sequencing and

Analysis Conference Miami Beach, Florida, USA September  
12-15, 2000

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

T1 Multiplexed genotyping assay that combines a novel labeling  
strategy with microchannel electrophoresis.

AB Genome-wide SNP scans to support large association studies and  
specific genotyping panels used for phenotype prediction are both  
requirements of new technologies. . . to comprehensively address  
emerging genotyping demands. By combining ACLARA's proprietary probe  
labeling strategy with existing, robust genotyping biochemistries such as  
TaqMan>TM we have designed a flexible, multiplexed assay  
format for analyzing nucleic acids in a broad spectrum of genomics needs.  
Genotyping applications using this assay format are. . . This assay  
configuration is uniquely characterized by its modular composition. Sets  
of electrophoretic mobility tags (e-TagsTM) "code" specific probes in  
multiplexed sets. These tags are released during amplification via  
TaqMan cleavage and subsequently separated by capillary  
electrophoresis. The electrophoretic pattern is "decoded" to yield a  
genotype. Initially, 20 e-Tags will be used to provide 10-plex genotyping  
capability during each capillary separation. The modular assay design  
allows a single genotyping multiplex to be applied to a large  
number of samples or, alternatively, parallel multiplex  
reactions can be done to assay many polymorphisms in a single sample.  
Multiplexed e-Tag genotyping data for the pharmacogenetics targets  
CYP2D6 and ApoE will be presented.

L6 ANSWER 18 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC. on STN

DUPLICATE 7

ACCESSION NUMBER: 1999:369986 BIOSIS

DOCUMENT NUMBER: PREV199900369986

TITLE: High-throughput genotyping method for glutathione  
S-transferase T1 and M1 gene deletions using TaqMan  
(R) probes.

AUTHOR(S): Shi, Michael M. (1); Myrand, Scott P.; Bleavins, Michael  
R.; de la Iglesia, Felix A.

CORPORATE SOURCE: (1) Pathology and Experimental Toxicology, Parke-Davis  
Pharmaceutical Research, Warner-Lambert Company, 2800  
Plymouth Rd., Ann Arbor, MI, 48105 USA

SOURCE: Research Communications in Molecular Pathology and  
Pharmacology, (Jan., 1999) Vol. 103, No. 1, pp. 3-15.  
ISSN: 1078-0297.

DOCUMENT TYPE: Article

LANGUAGE: English



SUMMARY LANGUAGE: English

TI High-throughput genotyping method for glutathione S-transferase T1 and M1 gene deletions using TaqMan(R) probes.

AB. . . glutathione-S-transferase theta and mu (GSTT1 and GSTM1). This method utilizes the 5'-nuclease activity of Taq polymerase in conjunction with fluorogenic TaqMan(R) probes. In contrast to traditional allelic discrimination genotyping to detect single nucleotide polymorphisms, the current assay has been designed to detect gene deletion by utilizing custom-designed TaqMan probes in conjunction with an exogenous internal positive control probe. The TaqMan genotyping results were validated by a commonly used multiplex PCR technique. Screening of 71 unrelated individuals revealed gene deletion (null) genotype of 15.5% and 40.8% for GSTT1 and GSTM1, respectively. This TaqMan genotyping method is rapid, reproducible, and highly sensitive and could be applied toward fully automated large-scale genotyping.